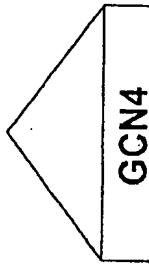
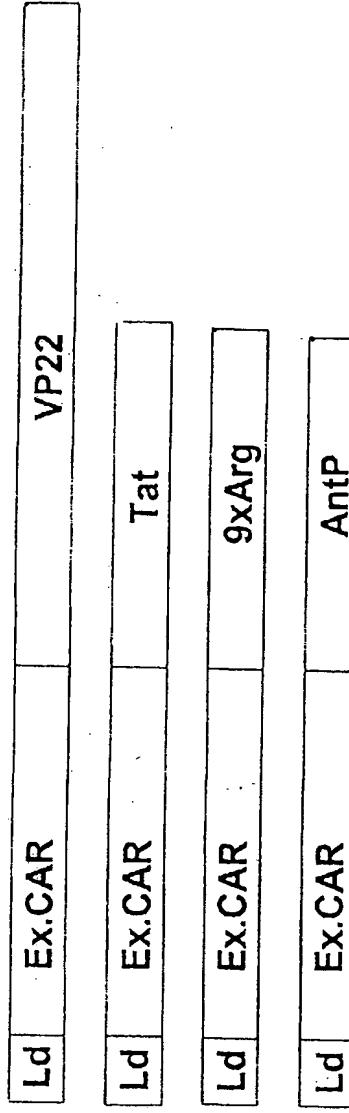
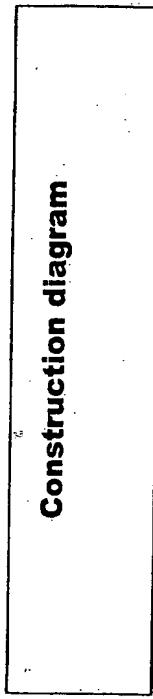


U.S. Patent Application No. 10/583,249
Inventor(s): Stephan KUBICKA
Filed: June 16, 2006 Art Unit: Not yet assigned
For: MEDIZINISCHE HOCHSCHULE HANNOVER
Attorney Docket: Q95566
Sughrue Telephone No.: 202-293-7060
REPLACEMENT DRAWING Fig. 1

Figure 1

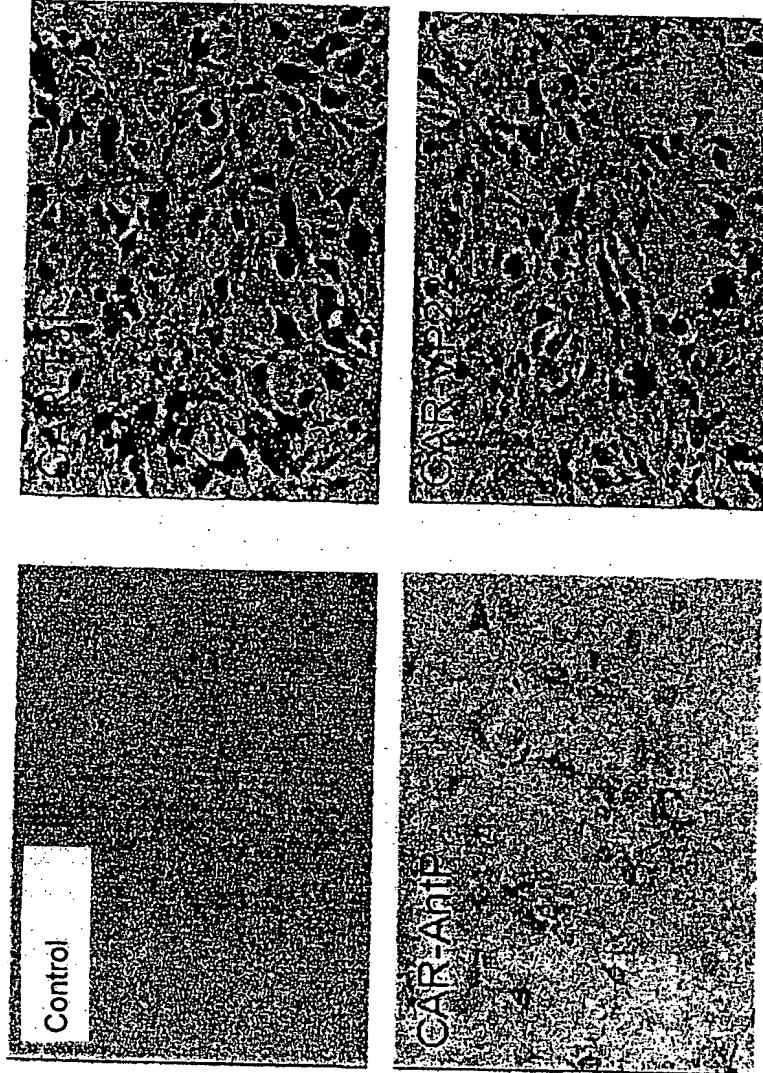
Construction diagram



Legend:

- Ld** = natural leader sequence of the coxsackie adenovirus receptor for synthesis of the protein into the endoplasmic reticulum
Ex.CAR = extracellular domain of the coxsackie adenovirus receptor
GCN4 = optional insertion of an oligomerization domain (here GCN4 as an example) for possible intensification of the CAR/fibre knob affinity

Figure 2



Fusion proteins from the extracellular domain of the Coxsackie adenovirus receptor and basic peptides or VP22 increase the adenoviral infection of CAR-deficient NIH3T3 fibroblasts.
293 cells were transfected with expression constructs for the fusion proteins shown in the figure (pBluescript as a control). After 36 h the supernatants of the cell layer were removed and mixed with LacZ-transgenic adenoviruses (Ad-LacZ). Thereafter, NIH3T3 fibroblasts were infected with this mixture. The multiplicity of infection (MOI) here was 10. After 48 h the infected NIH3T3 cell layer was analysed for β -galactosidase expression by blue staining by X-gal substrate conversion in order to demonstrate the viral infection

▷ = penton base
= fibre knob
= integrin

= CAR
= CAR fusion protein

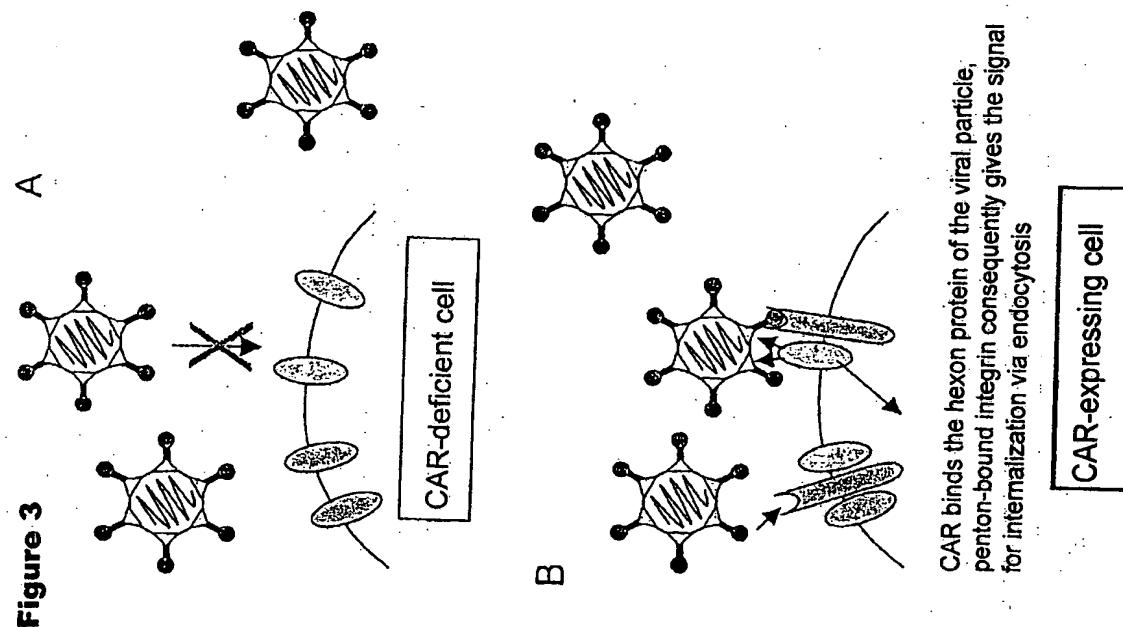
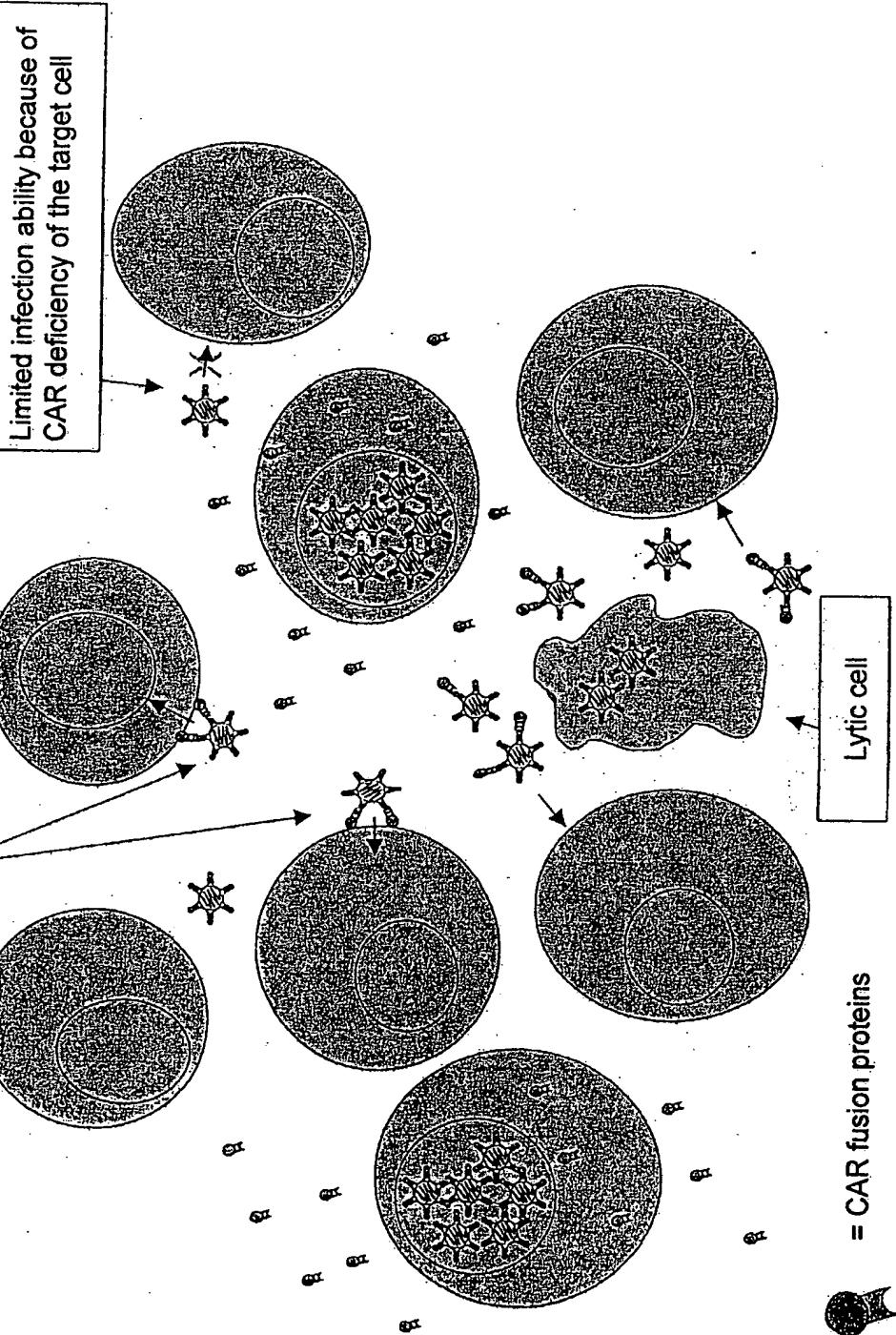


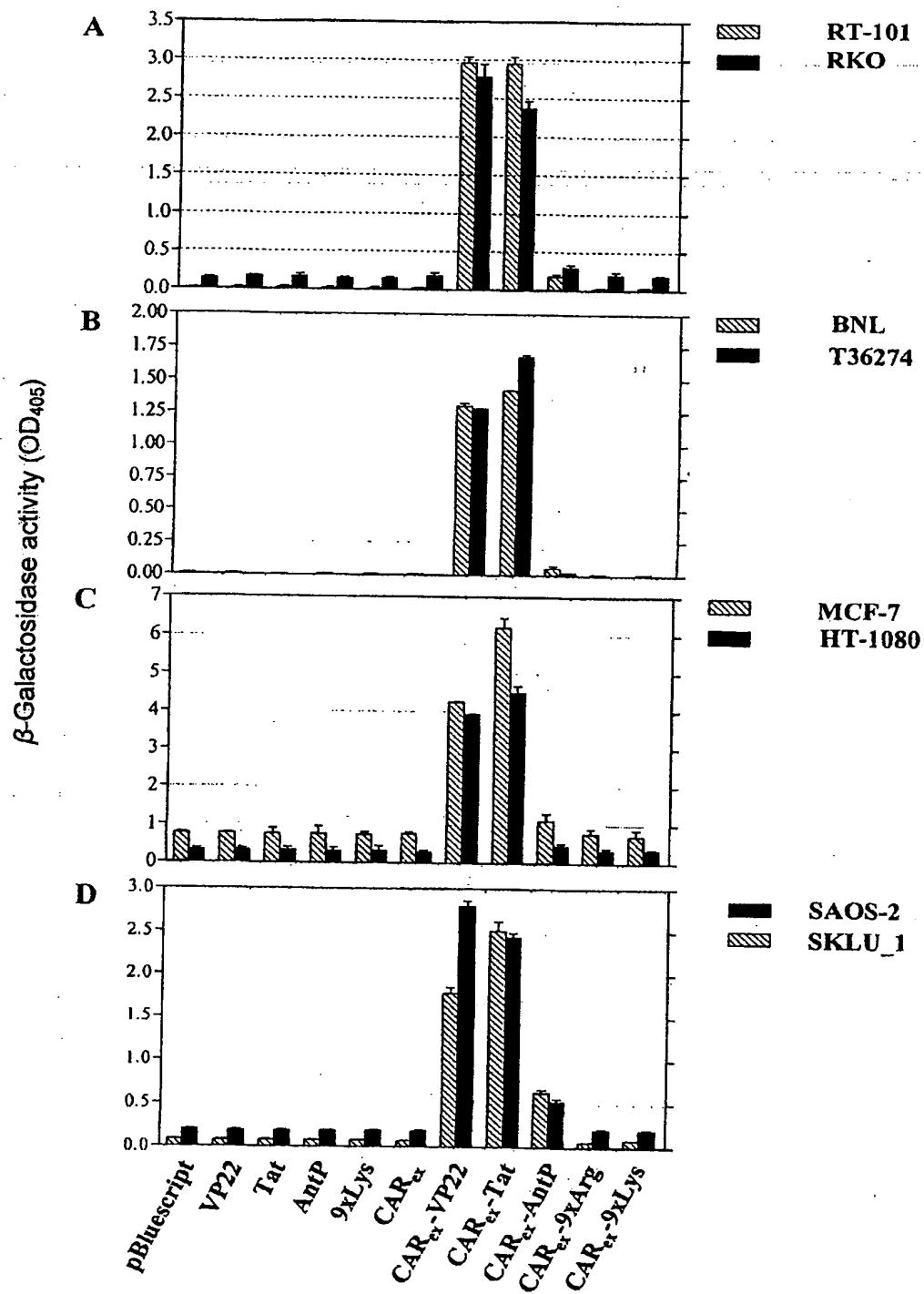
Figure 3

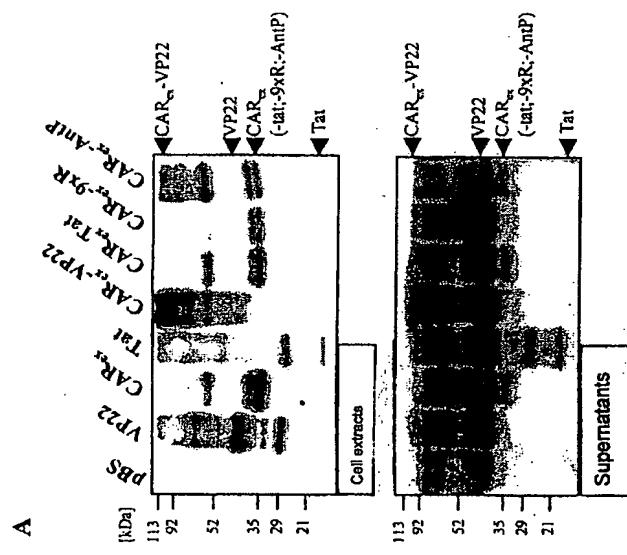
Figure 4

Infection processes mediated by CAR fusion protein



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Fig. 5: Infection efficiency of various cell lines



B

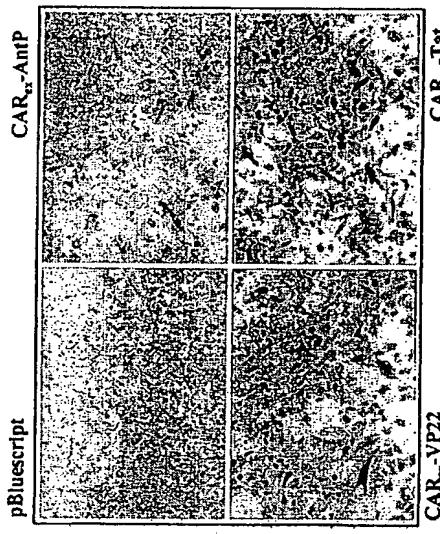


Fig. 6

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(MOI 10; 4 h infection)				
untreat. virus	+ CAR _α -Tat	+ CAR _α -VP22	+ CAR _α -Tat	
SAOS-2	0.5 - 2	45 - 55	50 - 65	
SKLU-1	~0	55 - 65	65 - 70	
MCF-7	2 - 3.5	40 - 50	50 - 60	
BNL	~0	15 - 20	15 - 20	
H4IIE	2 - 3	50 - 55	30 - 40	
HT1080	1 - 2	60 - 70	65 - 70	
RKO	0.5 - 1.5	65 - 75	60 - 70	
RT101	~0	15 - 25	15 - 25	
T-36274	~0	35 - 45	35 - 40	

av. transduction (%)

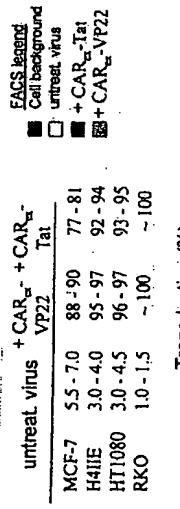
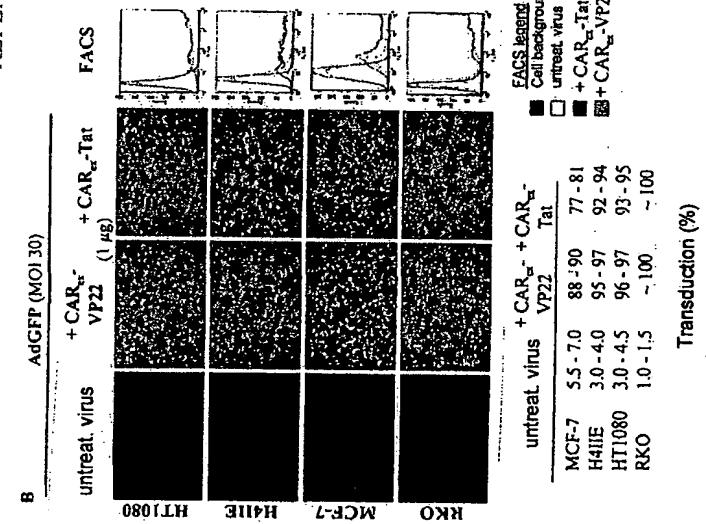


Fig. 7

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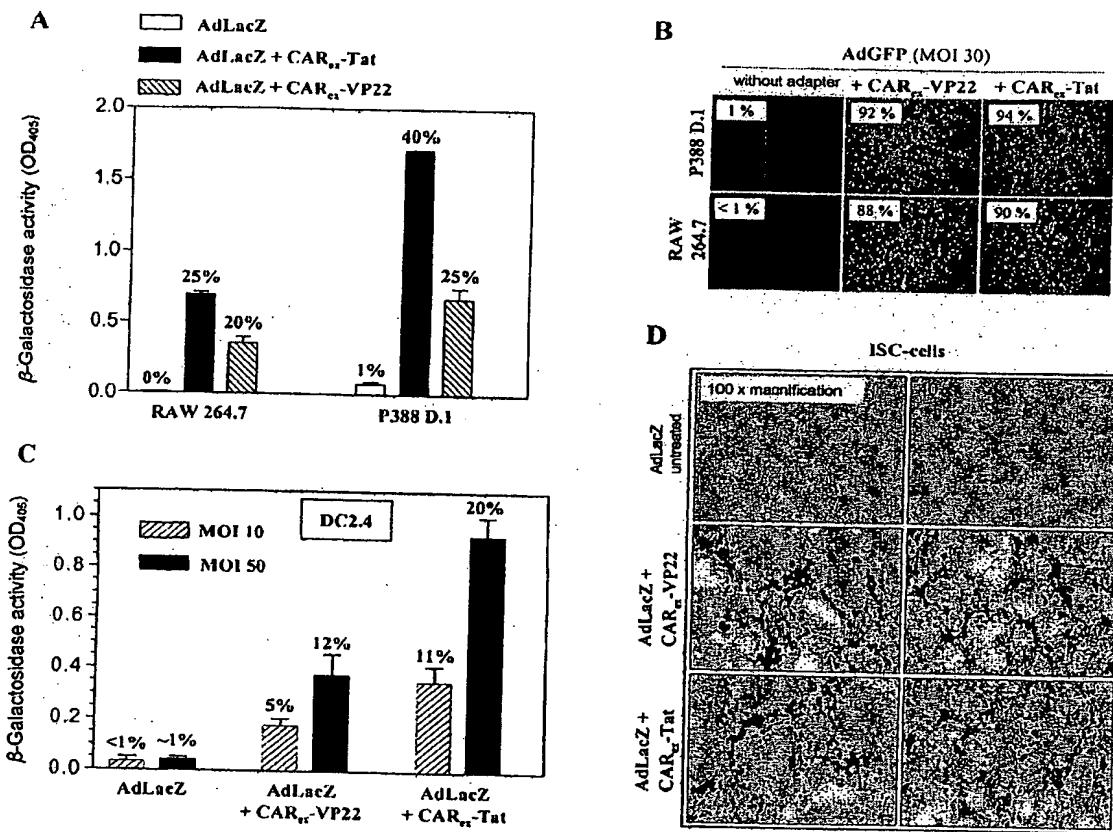


Fig. 8

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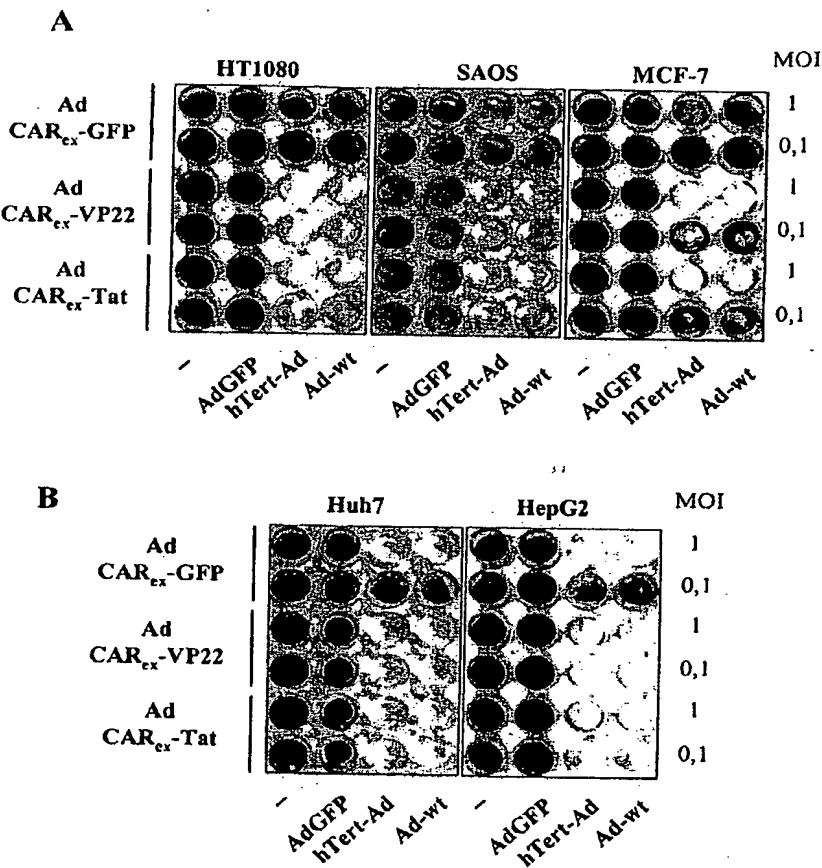


Fig. 9

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REPLACEMENT DRAWING Fig. 10

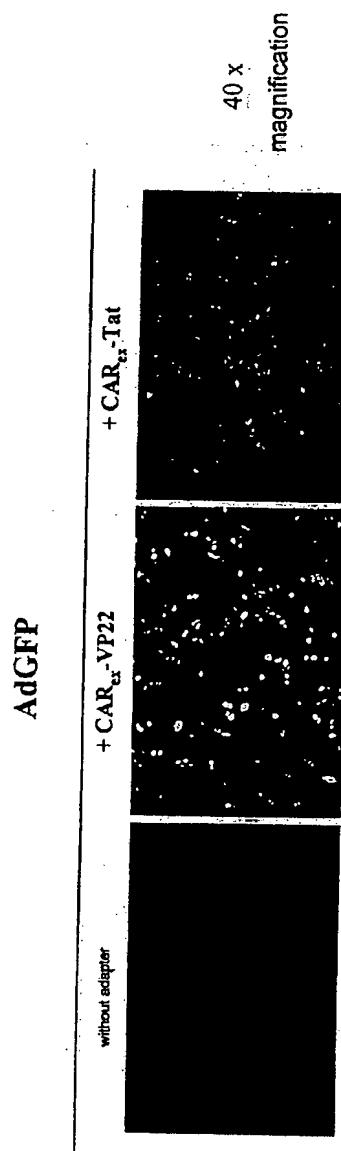


Fig. 10

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Fig. 11: Influence of the pH

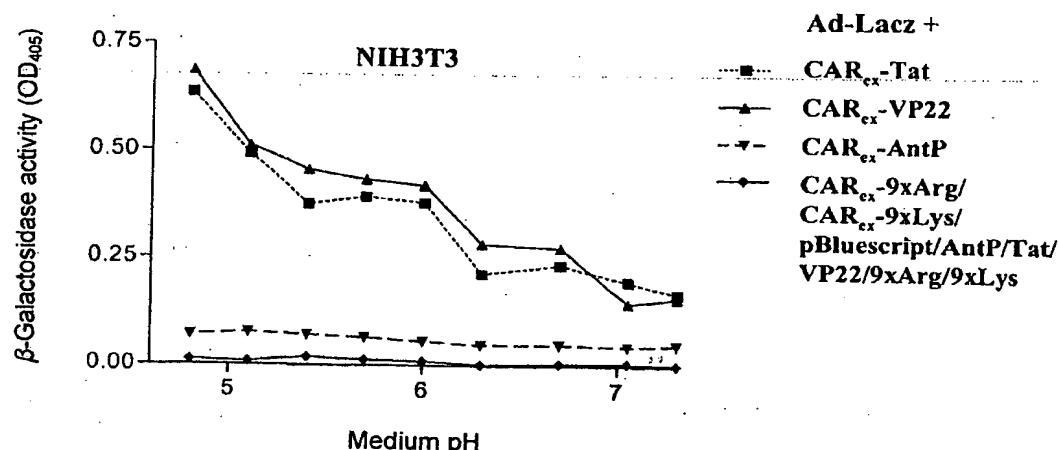
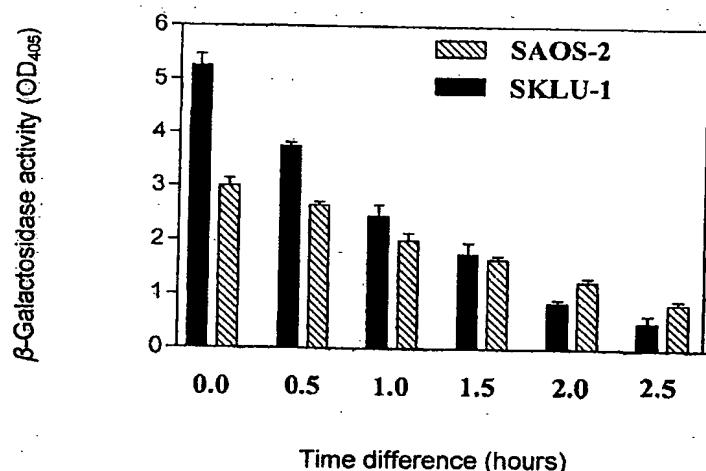


Fig. 12: Influence of the time delay



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